to guide management and take precautionary measures to alleviate negative outcomes.

Attention of these male patient should be paid to prevent the incidence of secondary osteoporosis.

Pediatric Endocrinology

PEDIATRIC ENDOCRINOLOGY: ADRENAL, THYROID, AND GENETIC DISORDERS

Impact of Male Hypogonadism on Bone Mineral Density in Childhood Hemato-Oncologic Disease

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Introduction: Patients with childhood hemato-oncologic diseases have many medical problems, not only due to disease itself, but also adverse effects of specific treatment that patients had. Osteoporosis, one of the most common side effects of the treatment, decreases quality of life when the disease progresses. Our study investigated the impact of male hypogonadism on secondary osteoporosis in childhood hemato-oncologic patients, using association between male sex hormone and bone mineral density (BMD) measured by dual energy X-ray absorptiometry (DXA). **Methods:** This study collected BMD score (T-score) of 52 male subjects who were diagnosed with hemato-oncologic diseases in the past (average age of 22.3 years at DXA examination). All subjects measured serum testosterone and we divided them into two subgroups according to gonadal status. The first group, called hypogondal group, was a group of subjects with serum testosterone level less than 3.5 ng/ml. The other group was classified into eugonadal group, with serum testosterone level equal or more than 3.5 ng/ml. Mean BMD score of spine and hip were presented and compared between the two groups. Furthermore, relativity with other risk factors for osteoporosis was calculated using multiple regression analysis. **Results:** Overall, spine BMD in the hypogondal group did not significantly differ from the eugonadal group. However, hip BMD was significantly lower in the hypogonadal group (mean difference; 0.8, $p = 0.023$). Furthermore, testosterone level itself showed linear correlation with BMD score in hip ($p = 0.013$). When other risk factors for osteoporosis were taken into account, hemato-oncologic patients treated with total body irradiation also had significantly lower hip BMD ($p = 0.007$) compared with non-irradiation group. Hypogonadism still remained a significant factor for decreased bone mineral density in hip ($p = 0.022$). **Conclusions:** Hemato-oncologic patients with hypogonadism or previously treated with total body irradiation are at increased risk of decreased bone mineral density in both hips. Hypogonadism alone remains independent risk factor for osteoporosis in hip.

Pediatric Endocrinology

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Novel Pathogenic Variants in LHX3, LHX4 and GLI2 Identified in Pediatric Patients With Congenital Hypopituitarism: From Variant Calling To Variant Testing

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Congenital hypopituitarism (CH), septo-optic dysplasia (SOD), and holoprosencephaly (HPE) constitute an important group of structural birth defects that cause significant morbidity and life-long consequences for quality of life and care. The genetic causes are highly overlapping. As such, these disorders can be considered as a spectrum of related disorders. Improved insight into genetic causes would be valuable for patients, families, and medical geneticists. Very few systematic genetic screens have been carried out for patients with CH. We implemented genetic screening using single-molecule molecular inversion probes sequencing to identify causative mutations in a set of 67 genes previously reported in CH patients and the spectrum encompassing SOD and HPE. We captured genomic DNA from 170 Argentinean pediatric patients with CH, and 54% of the patients in this cohort have craniofacial, ophthalmologic, and/or central nervous system defects. We found candidate pathogenic, likely pathogenic and variants uncertain significance (VUS) in 23% of the cases. In order to evaluate the functional consequences of VUS in *LHX3, LHX4*, and *GLI2*, we performed *in-vitro* functional assays to study the activity of the mutated proteins. To test *LHX3/4* variants we co-transfected HEK293T cells with wild type (WT) or mutated *LHX3/4* variant plasmids and luciferase reporter genes driven by the α*GSU* promoter or *GH1* promoter and assayed for luciferase activity. For *GLI2* functional analysis we used the cell line NIH/3T3-CG, stably transfected to express GFP under the presence of GLI2 activated form. Endogenous *Gli2* was knocked out by CRISPR-Cas9 and